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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/988,971	11/20/2001	Han Chang	D0043 NP	9658

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STEPHEN B. DAVIS
BRISTOL-MYERS SQUIBB COMPANY
PATENT DEPARTMENT
P O BOX 4000
PRINCETON, NJ 08543-4000

EXAMINER	
BELYAVSKYI, MICHAIL A	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 12/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/988,971	CHANG ET AL.	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-25,31,33-35 and 41-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-25,31,33-35 and 41-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/04/04 has been entered.

Claims 21-25, 31, 33-35 and 41-44 are pending.

Claims 21-25, 31, 33-35 and 41-44 are under consideration in the instant application.

In view of the amendment, filed 10/04/04 the following rejections remain:

2. 35 U.S.C. § 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

3. Claims 21-25, 31, 33-35 and 41-44 stand rejected under 35 U.S.C. 101 as the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility for the same reasons set forth in the previous Office Action, mailed 11/04/03.

Applicant's arguments, filed 05/06/04 have been fully considered, but have not been found convincing.

Applicant assets that : (i) one skilled in the art would reasonable believed that hSLAP-2 is a new member of the SLAP family of adapter proteins based upon the evidence provided in the instant specification , (ii) as stated in paragraph 76 of the instant specification that hSLAP-2 is a "negative regulator of intracellular signal transduction in several cell types including T cells; (iii) as disclosed by Pawson et al and Pandey et al, the presence of SH2/SH3 domain alone is sufficient evidence to demonstrate that hSLAP-2 is an adaptor protein ;(iv) claimed hSLAP-2 polynucleotide has a substantial utility that is exemplified by the fact that unregulated cellular proliferation and uncontrolled clonal expansion in B-cells can result in B-cell tumors, lymphomas and leukemias, (v) claimed hSLAP-2 polynucleotide have a well established utility due to its significant homology to known adaptor proteins, particularly SLAP family member and shared expression profile to other SLAP family member and pointed to the teaching of

Holland et al., Pandey et al and Loreto et al. Each of these assertions will be addressed individually.

First, as was stated in the previous Office Action, the specification disclosed a novel nucleic acid molecules of SEQ ID NO: 1 encoding SH2/SH3 domain –containing protein h SLAP-2 of SEQ ID NO:2. The specification fails to provide sufficient objective evidence of any activity for encoded protein. Applicant only states that said protein shows 47 % identity to human SLAP and 58 % identity to the mouse SLAP proteins (see Table 4 and page 61, lines 22-30 in particular). The specification disclosed that based on sequence homology to related molecules , said protein may be a novel human SLAP-2 protein. The specification also disclosed that said hSLAP-2 nucleic acid sequence and related protein can be used for diagnosing, treating or preventing disorders or diseases associated with aberrant or uncontrolled cellular signal transduction or with hyperactive cell, or may play a role in one or more aspects of regulating the immune system and tumor cell biology (see page 20, lines 5-20 and page 41, lines 22-30 in particular). No well-established utility for a human SLAP-2 protein is indicated. Moreover, in addition to previously cited references indicating that homology –based prediction of protein function is unreliable, newly cited references of Whisstock et al., (Quarterly Review of Biophysics, 2003, 36, pp307-340) teaches that prediction of protein function from sequence and structure is difficult problem, because homologous proteins often have different function. A fundamental problem is that function is in many cases an ill-defined concept (see Abstract in particular). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). Thus, in light of the art recognized fact that minor sequence differences can significantly affect a protein's function, one skilled in the art would find it more likely than not that h SLAP-2 of SEQ ID NO:2 is not having the same function as human SLAP. The recitation of percent identity language, in the absence of *a testable function* and limitations regarding the *sequence length over which the percent identity is required* does not allow the skilled artisan reasonable believed that hSLAP-2 is a new member of the SLAP family of adapter proteins. Thus, the homology-based assignment h SLAP-2 of SEQ ID NO:2 as human SLAP receptor does not appear to provide evidence of a specific and substantial utility based on the knowledge of the skilled artisan and the data presented in the instant specification.

Second, in paragraph 76 of the instant specification it is clearly stated that SLAP, not hSLAP-2, have been shown to be a negative regulator of intracellular signal transduction in several cell types including T cells.

With regard to the teaching of Pawson et al., and Pandey et al, the Examiner disagree with the Applicants interpretation of said references. Pawson et al., merely teach role of scaffold, ancoring and adaptor proteins that contribute to the specificity of signal transduction events by recruiting active enzymes into signaling network (see entire document, Abstract in particular). Moreover, Pawson et al., teach that different types of proteins may have several interacting domains including PDZ, SH3 and LIM domains and that covalent associating of these recognition modules as found in adaptor ancoring and docking proteins allows a single peptide to

bind multiple protein ligands. As an added complexity a single module can bind either to a motif within the same molecule or in an intermolecular fashion to other proteins (see page 2079 in particular). Similary, Pandey et al. teach that adapter proteins contain a variety of modular domains that mediate protein-protein interaction and further that a number of adapter proteins have been isolated , some of them have positive regulation while others have negative regulation (see entire document, page 19131 in particular. No single effect of the disclosed hSLAP-2 is ascribed to the claimed protein and the original members of the family were not classified based on their biological activity, but rather, by their common structure and the fact that they are adaptor proteins. Without some common biological activity for the family members, a new member would not have a specific, substantial, or credible utility when relying only on the fact that it has structural similarity to the other family members and is also a adaptor protein. The members of the family have different biological activities which are related to regulation of intracellular signal transduction in several cell types including T cells, but there is no evidence that the claimed compounds share any one of those activities. The rejection was based on the failure to disclose sufficient properties of SH2/SH3 domain –containing protein h SLAP-2 of SEQ ID NO:2 to support an inference of utility. The adaptor subfamily to which the polypeptide belongs is a family in which the members have divergent functions. Assignment to this family does not support an inference of utility because the members are not known to share a common utility. To argue that all the members can be used for "regulation" of intracellular signal transduction in several cell types including T cells is to argue a general, nonspecific utility that would apply to virtually every member of the family, absent evidence to the contrary. Further, any compound could be considered as regulator or modulator of a tissue in that any compound, if administered in the proper amount, will stimulate or inhibit a tissue. For example, salt, ethanol, and water are all compounds which will kill cells if administered in a great enough amount, and which would stimulate cells from which these compounds had been withheld, therefore, they could be considered regulators or modulators of epithelial tissue. However, use of these compounds for the modulation of epithelial tissue would not be considered a specific and substantial utility unless there was some disclosure of, for example, a specific and particular combination of compound/composition and application of such in some particular environment of use.

With regards to the fact that unregulated cellular proliferation and uncontrolled clonal expansion in B-cells can result in B-cell tumors, lymphomas and leukemias. This arguments is not disputed, however, the issue raised by the Examiner in the previous Office Action was that the specification does not disclose any diseases or conditions known to be associated with the hSLAP polypeptide , encoded by SEQ ID NO:2 or any conditions associated with altered levels (increase or decrease) of said polypeptide. Since any protein may potentially be used as a treatment agent, this utility would not be considered to be specific. Since no particular disease or condition is disclosed, the artisan would have been required to perform additional experimentation to identify and/or reasonably confirm the asserted use of hSLAP polypeptide as a treatment agent and therefore, this utility would not be considered to be substantial.

With regards to the teaching of Holland et al., Pandey et al and Loreto et al. , that hSLAP-2 polynucleotide have a well established utility due to its significant homology to known adaptor

proteins, particularly SLAP family member . Although said papers teach that hSLAP-2 protein may have similarities to SLAP nowhere in said papers there are indications or teaching that hSLAP-2 indeed have the same function as SLAP protein. Moreover, Holland et al., teach that although SLAP-2 and SLAP share structural homologies their mechanisms of action is different and further studies are required to determine the role and function of SLAP-2 protein (see overlapping pages 1273 –1274 in particular). Similarly, Pandey et al. teach that C terminus of SLAP-2 is not very similar to that of SLAP ant it lacks the last 27 amino acid found in SLAP (see page 19137 in particular). Thus, after further research, specific and substantial utility might be found for claimed polypeptide h SLAP-2 of SEQ ID NO:2. This further characterization, however is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. A well-established utility is a specific, substantial, and utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material.

As such, further research would be required. See Brenner v. Manson, 383 U.S. 519, 535-36, 148 USPQ 689, 696 (1966), the court indicates "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." A patent is therefore not a license to experiment. Because the claimed invention is not supported by a specific asserted utility for the reasons set forth, credibility of any utility cannot be assessed.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 21-25, 31, 33-35 and 41-44 stand also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial, asserted utility or a well established utility for the reasons set forth in the rejection under 35 USC101 above, one skilled in the art clearly would not know how to use the claimed invention for the same reasons set forth in the previous Office Action, mailed 11/04/03.

Applicant's arguments, filed 05/06/04 have been fully considered, but have not been found convincing.

Applicant argue that since hSLAP-2 has a specific, substantial and well established utility, one skilled in the art clearly would know how to use the claimed invention.

Contrary to Applicant's arguments as was stated above under 35 USC101 , it is the Examiner position that the claimed invention is not supported by either a specific and substantial, asserted utility or a well established utility thus one skilled in the art clearly would not know how to use the claimed invention.

6. No claim is allowed

7. This is a RCE of applicant's earlier Application No. 09/988971 . All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/272-0841.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michail Belyavskyi, Ph.D.
Patent Examiner
Technology Center 1600
December 20, 2004